



Herpes Simplex & Genital Warts

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Learning Objectives

- Describe the epidemiology of genital HSV in KSA.
- Describe the pathogenesis of genital HSV.
- Discuss the clinical manifestations of genital HSV.
- Identify the common methods used in the diagnosis of genital HSV.
- Describe patient management for genital HSV.

What is genital herpes?

- Genital herpes is a sexually transmitted disease caused by the herpes simplex viruses (HSV) type 1 and type 2.
- **Herpes simplex virus 1 and 2 (HSV-1 and HSV-2)**, also known as **human herpesvirus 1 and 2 (HHV-1 and HHV-2)**.

Introduction

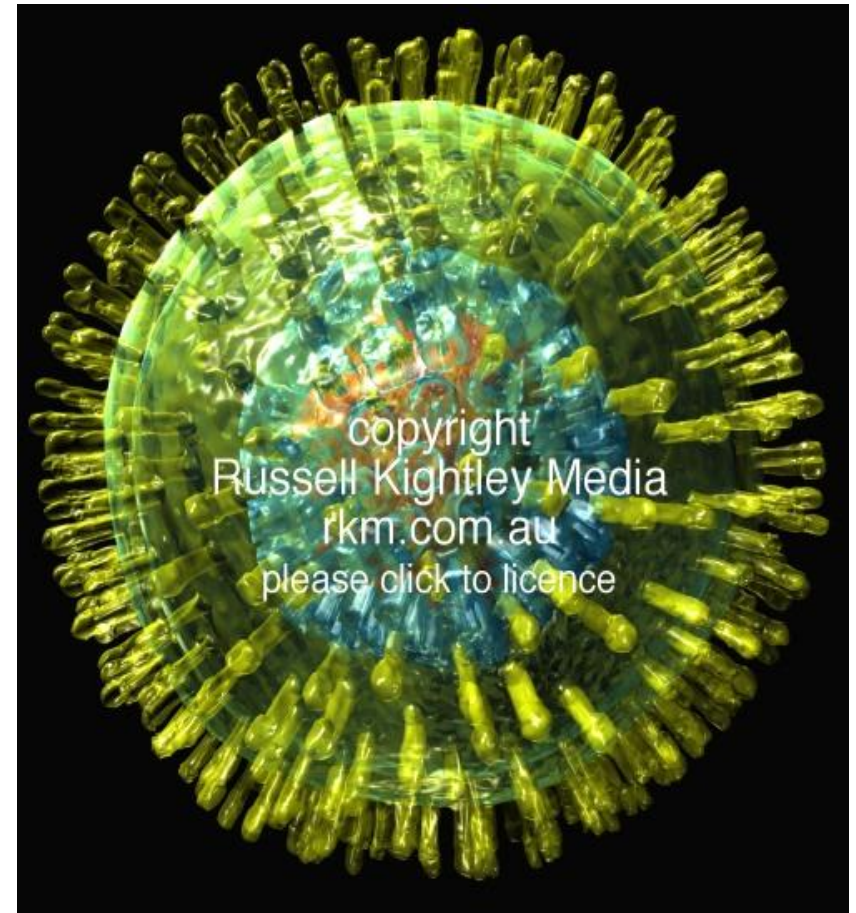
- Herpes viruses are a leading cause of human viral diseases, second only to influenza and cold viruses.
- Are capable of causing overt disease or remaining silent for many years only to be reactivated .
- Name Herpes comes from the Latin herpes which was comes from the Greek word herpein means to creep.

Types of Herpesviruses

- **Herpes simplex virus (HSV-1, HSV-2).**
- **Varicella-Zoster virus (VZV).**
- **Epstein-Barr virus (EBV).**
- **Cytomegalovirus (CMV).**
- **Human herpesvirus 6 (HHV6).**
- **Human herpesvirus 7 (HHV7).**
- **Human herpesvirus 8 (HHV8).**

Morphology

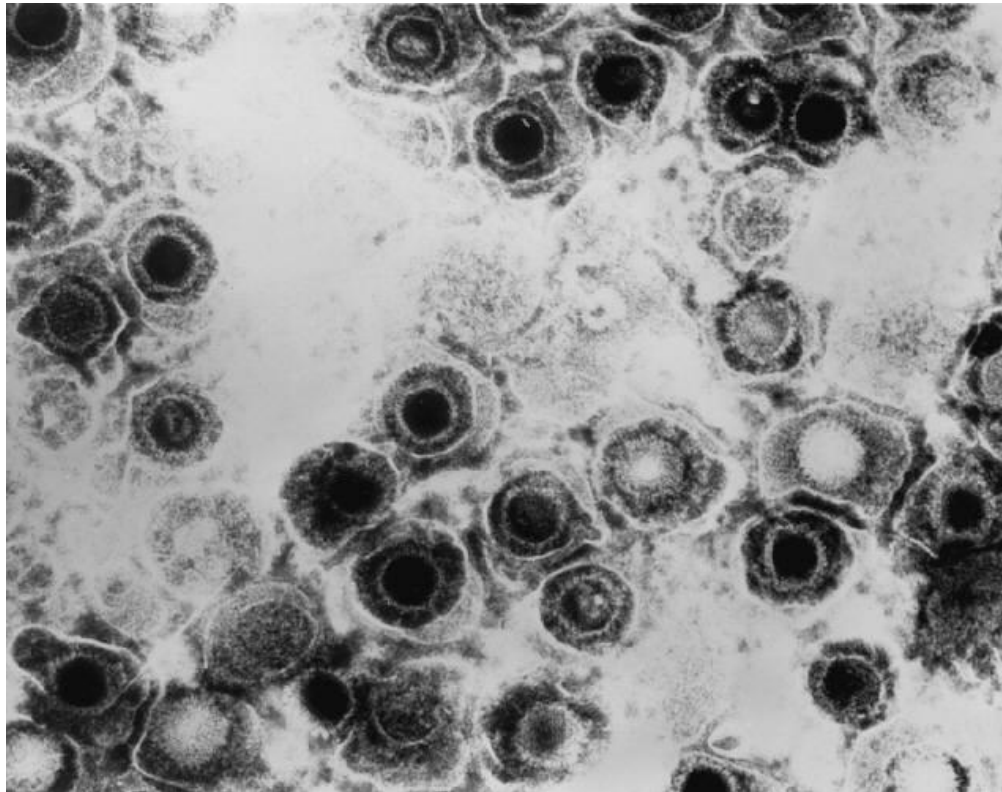
- 100 – 200 nm diameter, contains an icosahedral capsid containing linear double stranded DNA genome.
- Surrounded by a lipid envelope containing peplomers.
- Between capsid and envelope is tegument



Herpes Simplex Virus (HSV)

- Very large viruses and their genome (150 kb) encodes at least 80 proteins.
- Almost any human cell type can be affected by HSV.
- The genome of HSV-1 and HSV-2 share 50 - 70% homology.
- Man is the only natural host.
- HSV-1 is usually associated with oral and ocular lesions.
- HSV-2 is responsible for the majority of genital infections

Transmission electron micrograph of Herpes Simplex Virus



Virus classification

Group:	Group I (<u>dsDNA</u>)
Order:	<u>Herpesvirales</u>
Family:	<u>Herpesviridae</u>
Subfamily:	<u>Alphaherpesvirinae</u>
Genus:	<u>Simplexvirus</u>

Species

Herpes simplex virus 1 (HSV-1)

Herpes simplex virus 2 (HSV-2)

Background and Burden of Disease

- Genital herpes is a chronic, lifelong viral infection.
- Two HSV serotypes – HSV-1 & HSV-2
- HSV-2 causes most cases of recurrent genital herpes in the U.S.
- Approximately 776,000 new cases occur each year

Background and Burden of Disease

(continued)

- In the U.S., 16.2% of adults aged 14–49 years have HSV-2 antibodies
- HSV-2 antibodies are not routinely detected until puberty
- HSV-2 seroprevalence is higher in women than men in all age groups and varies by race/ethnicity.
- HSV-1 IgG antibodies (93.2%) was found in those mothers who were not educated. (2007)
- The prevalence of HSV-2 IgG was higher among civil servants and teachers (40.0 % and 14.7 % respectively)

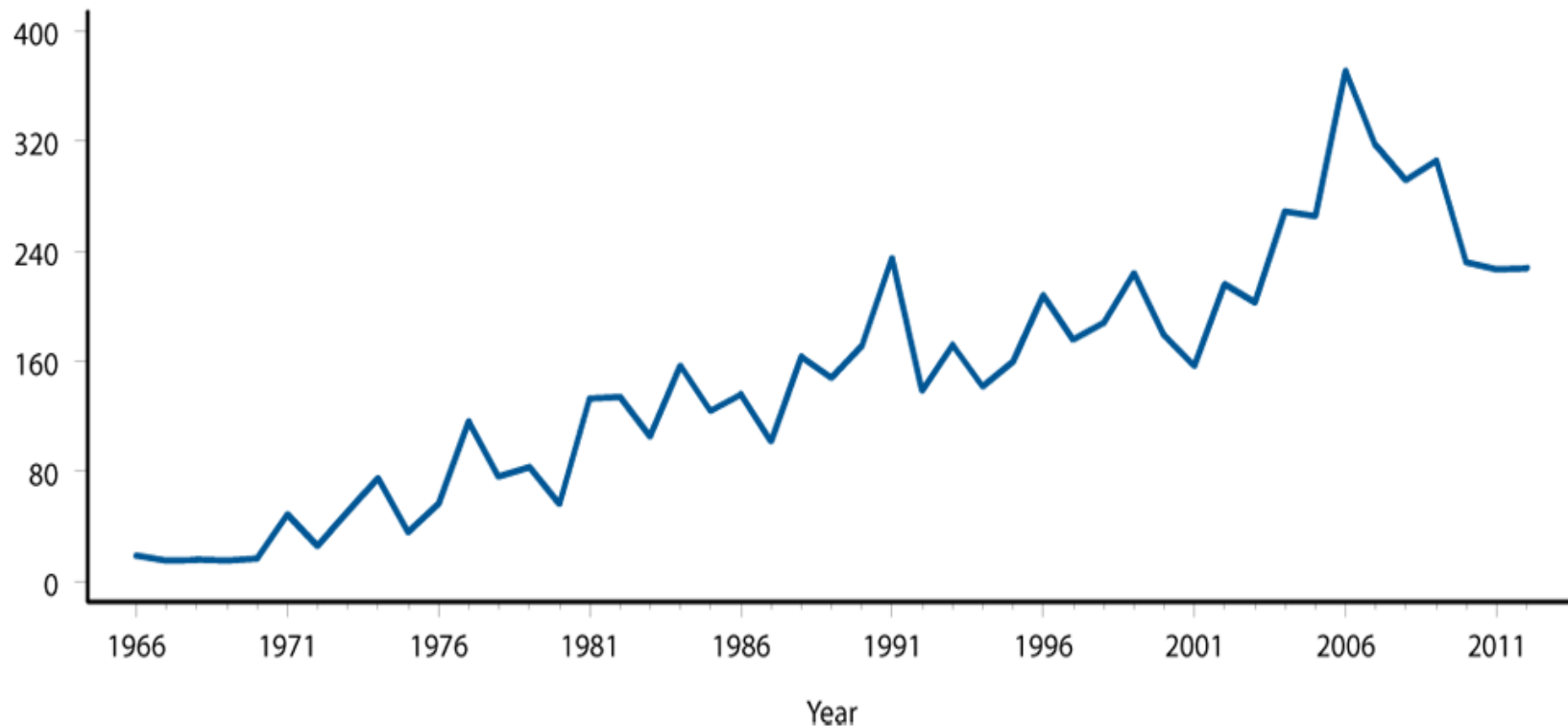
HSV-1 & HSV-2

Similar in morphology & structure, but can be distinguished by the following:

- **Location of the lesion:**
 - HSV-1 above the waist
 - HSV-2 below the waist.
- **Antigenicity:** differentiated by type-specific monoclonal antibodies.
- **Restriction endonuclease pattern** of their genome DNA.

Genital Herpes — Initial Visits to Physicians' Offices, United States, 1966 – 2012

Visits (in thousands)



NOTE: The relative standard errors for genital herpes estimates of more than 100,000 range from 18% to 30%.

SOURCE: IMS Health, Integrated Promotional Services™. IMS Health Report, 1966 – 2012

Symptoms

General symptoms may include:

- Decreased appetite
- Fever
- General sick feeling (Malaise)
- Muscle aches in the lower back or knees
- Swollen and tender lymph nodes during an outbreak
- Genital symptoms include the appearance of small, painful blisters filled with clear fluid.
- In women: on the outer vaginal lips (labia), vagina, cervix, around the anus, and on the thighs or buttocks

Transmission

- HSV-2 is transmitted sexually and perinatally
- Most genital herpes infections are transmitted by persons who are
 - unaware they are infected with HSV-2 or
 - asymptomatic when transmission occurs
- Efficiency of sexual transmission is greater from men to women than from women to men

Transmission (continued)

- Likelihood of transmission declines with increased duration of infection
- Incubation period after acquisition is 2–12 days (average is 4 days)
- Drying and soap and water readily inactivate HSV; fomite transmission unlikely

HSV-2 and HIV Infection

- HSV-2 infection increases the risk of acquiring HIV infection at least 2-fold
- HSV-2 infection is also likely to facilitate transmission of HIV infection from persons co-infected with both viruses

Virology

- HSV-1 and HSV-2 are members of the human herpes viruses (herpetoviridae)
- All members of this species establish latent infection in specific target cells
- Infection persists despite the host immune response, often with recurrent disease

Pathogenesis

Source of infection

- Saliva, skin lesions or respiratory secretions from patients or carriers.

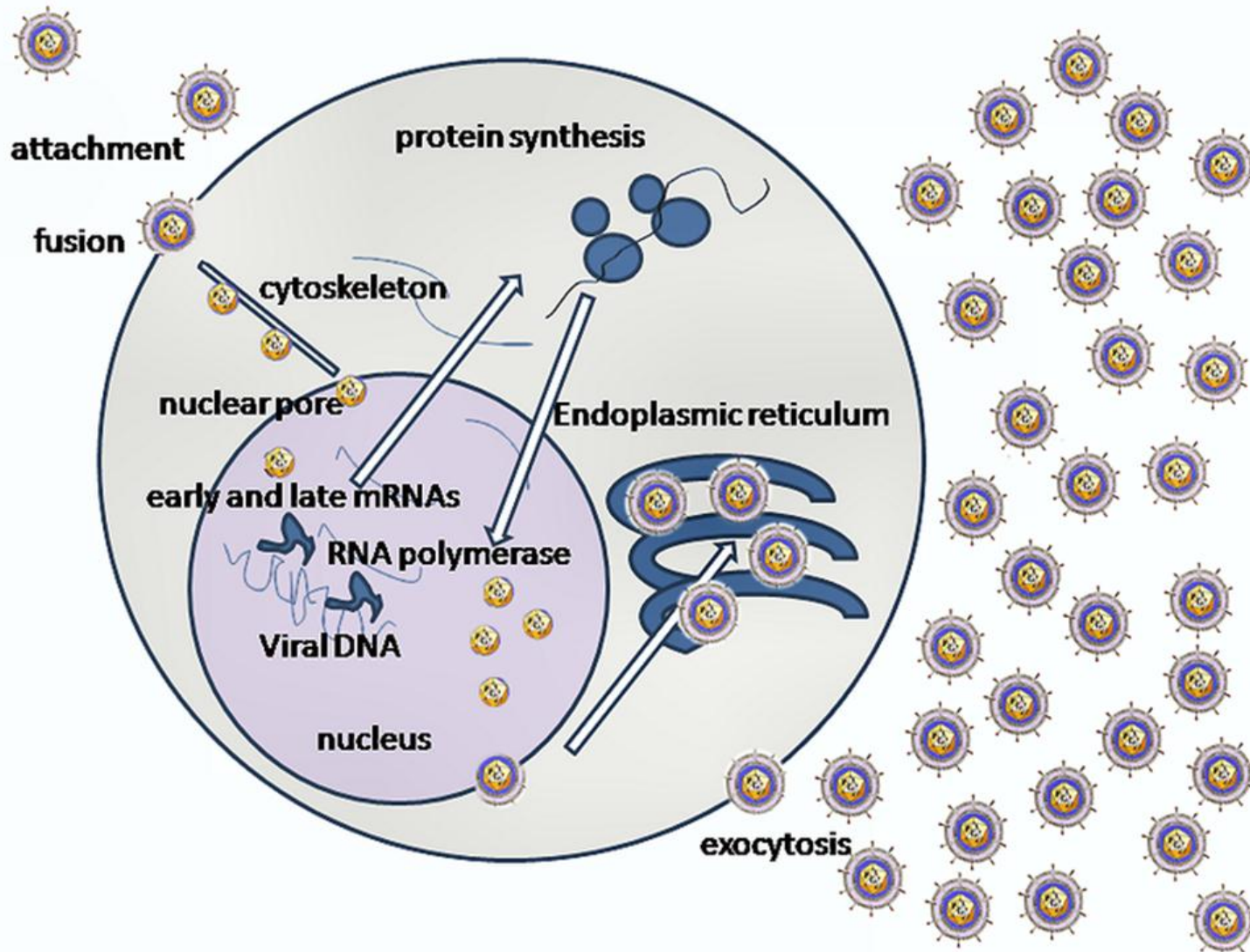
Mode of transmission

- Direct contact with virus containing secretions or with lesions
- HSV 1: Kissing or saliva contaminated fingers
HSV 2 : Sexual intercourse, congenital infection

Pathogenesis

- The virus remains latent indefinitely
- Reactivation is precipitated by multiple known and unknown factors and induces viral replication
- The re-activated virus may cause a cutaneous outbreak of herpetic lesions or subclinical viral shedding
- Up to 90% of persons seropositive for HSV-2 antibody have not been diagnosed with genital herpes

HSV Life Cycle



Definitions of Infection Types

First Clinical Episode

➤ Primary infection

- First infection **ever** with either HSV-1 or HSV-2.
- No antibody present when symptoms appear.
- Disease is more severe than recurrent disease.

➤ Non-primary infection

- Newly acquired HSV-1 or HSV-2 infection in an individual previously seropositive to the other virus.
- Symptoms usually milder than primary infection.
- Antibody to new infection may take several weeks to a few months to appear.

Definitions of Infection Types

Recurrent symptomatic infection

- Antibody present when symptoms appear
- Disease usually mild and short in duration.

Asymptomatic infection

- Serum antibody is present
- No known history of clinical outbreaks

Recurrent Infection Without Treatment

- Prodromal symptoms are common (localized tingling, irritation) - begin 12–24 hours before lesions
- Illness lasts 4–6 days
- Symptoms tend to be less severe than in primary infection
- Usually no systemic symptoms
- HSV-2 primary infection more prone to recur than HSV-1

Diseases caused by HSV-1

- 1. Acute gingivostomatitis .
- 2. Herpes labialis.
- 3. Keratoconjunctivitis.
- 4. Eczema herpeticum .
- 5. Encephalitis .
- 6. Dendritic keratitis

Diseases caused by HSV-2

- 1. Genital herpes (penis, urethra, cervix, vulva, vagina).
- 2. Neonatal herpes.
- 3. Aseptic meningitis.

Note: Besides above mentioned primary infections, herpesviruses may present as latent infection, reactivation and recrudescence

Genital Herpes: Primary Lesions



Genital Herpes: Multiple Ulcers



Genital Herpes: Recurrent Ulcer

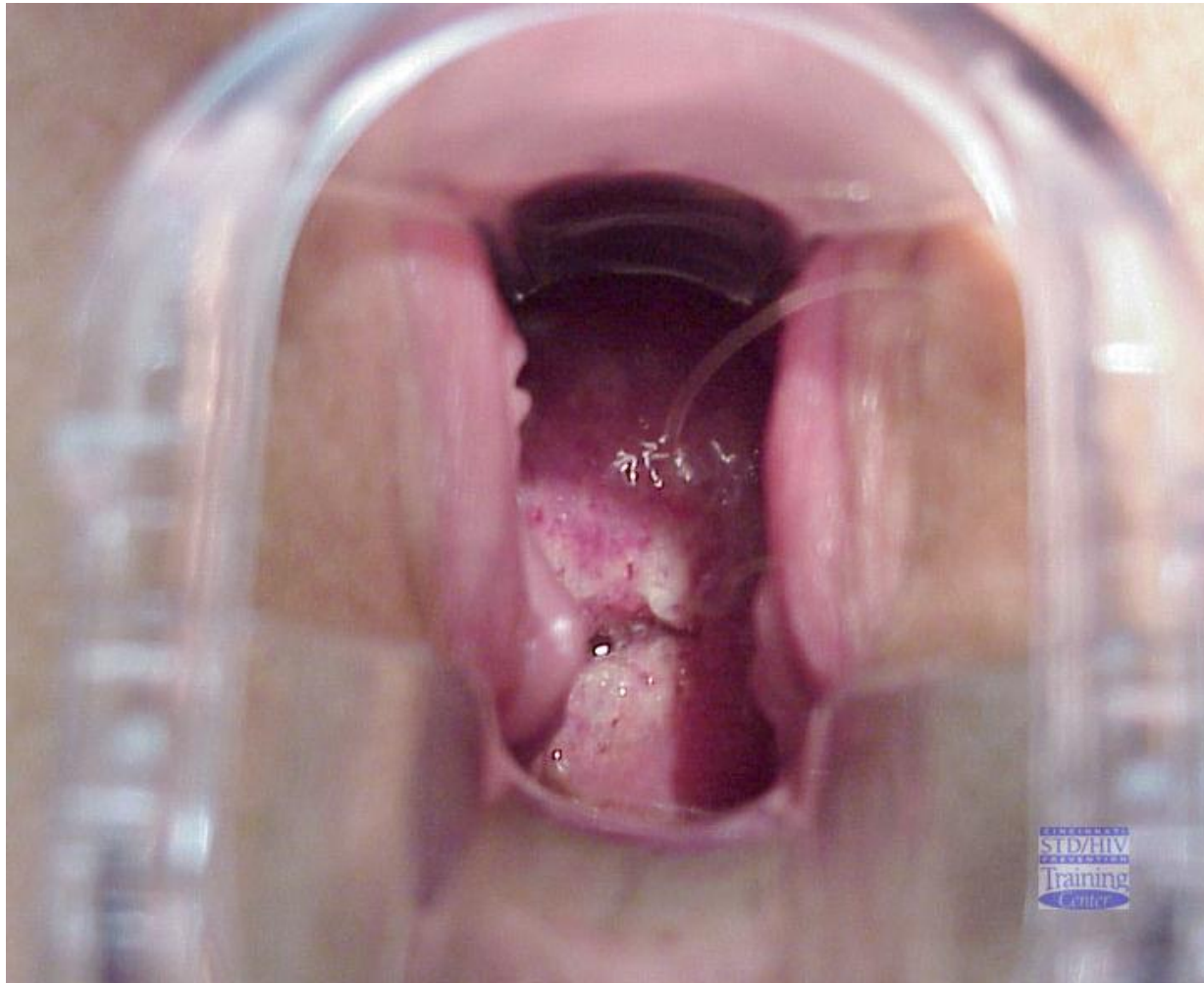


Genital Herpes: Periurethral Lesions



Source: Cincinnati STD/HIV Prevention Training Center

Genital Herpes: Cervicitis

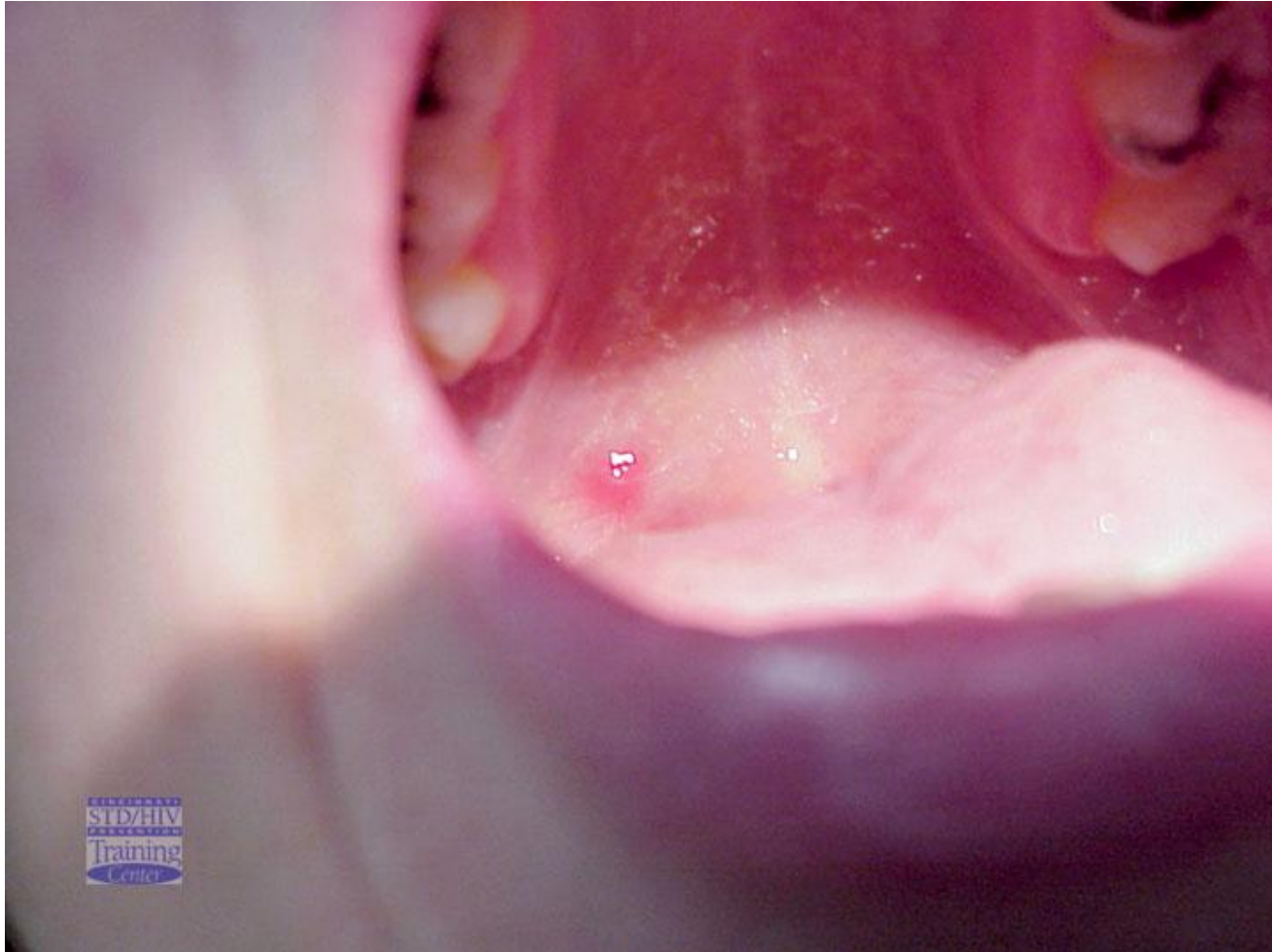


Source: Cincinnati STD/HIV Prevention Training Center

Herpes on the Buttock



Oral Herpes: Soft Palate



Asymptomatic Viral Shedding

- Most HSV-2 is transmitted during asymptomatic shedding
- Rates of asymptomatic shedding are greater in HSV-2 than HSV-1
- Rates of asymptomatic shedding are highest in new infections (<2 years) and gradually decrease over time
- Asymptomatic shedding episodes are of shorter duration than shedding during clinical recurrences

Asymptomatic Viral Shedding (continued)

- Most common sites of asymptomatic shedding are vulva and perianal areas in women and penile skin and perianal area in men
- Antiviral suppressive therapy dramatically reduces, but does not completely eliminate shedding

Complications of Genital Infection

- Aseptic meningitis
 - More common in primary than recurrent infection.
 - Generally no neurological sequelae.

- Rare complications include:
 - Stomatitis and pharyngitis.
 - Transverse myelitis.
 - Autonomic dysfunction.

HSV Diagnosis

- Clinical diagnosis is insensitive and nonspecific
- Clinical diagnosis should be confirmed by laboratory testing:
 - ❑ Virologic tests
 - ❑ Type-specific serologic tests

Virologic Tests

➤ Viral culture (gold standard)

- ☐ Preferred test if genital ulcers or other mucocutaneous lesions are present
- ☐ Highly specific (>99%)
- ☐ Sensitivity depends on stage of lesion; declines rapidly as lesions begin to heal
- ☐ Positive more often in primary infection (80%–90%) than with recurrences (30%)
- ☐ Cultures should be typed

➤ Polymerase Chain Reaction (PCR)

- ☐ More sensitive than viral culture; has been increasingly used instead of culture in many settings
- ☐ May be a reasonable choice for diagnosing genital lesions; the assays are FDA-cleared for use with anogenital specimens and commercially available
- ☐ Preferred test for detecting HSV in spinal fluid

Virologic Tests

(continued)

➤ Antigen detection

- ☐ Moderately sensitive (>85%) in symptomatic shedders
- ☐ Rapid (2–12 hours)!!!!
- ☐ May be better than culture for detecting HSV in healing lesions

➤ Cytology (Tzanck or Pap)

- ☐ Insensitive and nonspecific and should not be relied on for HSV diagnosis

Type-specific Serologic Tests

- Type-specific and nonspecific antibodies to HSV develop during the first several weeks to few months following infection and persist indefinitely
- Presence of HSV-2 antibody indicates anogenital infection
- Presence of HSV-1 does not distinguish anogenital from orolabial infection

Study resources

- Mim's Medical microbiology WW.CDC.gov.
- Medscape.com.
- WHO.int.org
- <http://www.skinsight.com/adult/sacralHerpesSimplexVirusHSV.htm>

Thank you

Question ?